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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,006	01/07/2002	Lothar Eggeling	PT 1.1678	7184

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EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 10/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,006	EGGELING ET AL.	
	Examiner	Art Unit	
	Christian L. Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-26 and 29-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-26 and 29-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The restriction requirement in the previous Office Action dated 12/22/2004 has been withdrawn in view of applicants' arguments filed 03/25/2005.

2. Claims 14-26 and 29-40 are pending and under consideration in this Office Action.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

3. Claims 14-26 and 29-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the evaluation of the claims for compliance with the written description requirement of 35 U.S.C. 112, of particular relevance is 66 FR 1099, Friday, January 5, 2001,which states:

> "*Eli Lilly* explains that a chemical compound's name does not necessarily convey a written description of the named chemical compound, particularly when a genus of compounds is claimed. *Eli Lilly,* 119 F.3d at 1568, 43 USPQ2d at 1405. The name, if it does no more than distinguish the claimed genus from all others by function, does not satisfy the written description requirement because "it does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. *Eli Lilly,* 119 F.3d at 1568, 43 USPQ2d at 1406. Thus *Eli Lilly* identified a set of circumstances in which the words of the claim did not, without more, adequately convey to others that applicants had possession of what they claimed." (see p. 1100, 1st column, line 47 to 2nd column, line 2).

Applicants' arguments filed 03/25/2005 have been fully considered but they are not persuasive. The examiner respectfully disagrees with applicants' arguments that the specification provides adequate written description of the claimed methods and adequate written description of regulatory elements and untranslated regions for reasons of record as supplemented below.

The claims are a genus claim that encompasses any microorganism transformed with a genus of ilvD genes encoding dihydroxy acid-dehydratases, a genus of ilvBN genes encoding acetohydroxy acid synthases, and a genus of ilvC genes encoding isomeroreductases, where the genes are from any biological source not limited to *Corynebacterium*, have any nucleotide sequence and structure, and include all variants and mutants thereof. Furthermore, the recited microorganism encompasses a genus of panB genes, a genus of panC genes, a genus of pane genes, and a genus of panD genes of any nucleotide sequence and structure from any *Corynebacterium* species including all variants and mutants thereof which are reduced or eliminated.

The scope of each genus includes many members from different biological sources with widely differing structural, chemical, and physical characteristics. Furthermore, each genus is highly variable because a significant number of structural differences between genus members exits.

While the specification provides a written description for a dihydroxy acid dehydratase of SEQ ID NO: 2 encoded by SEQ ID NO: 1, ketopantoate hydroxymethyl transferase of SEQ ID NO: 4 encoded by SEQ ID NO: 3, and pantothenate ligase of SEQ ID NO: 5 encoded by SEQ ID NO: 3 from Corynebacterium glutamicum, the recitation of the names such as "ilvD gene", "ilvBNC gene", and "panB" do not define any structural features and nucleotide sequences commonly possessed by each genus. Furthermore, while the specification discloses complementation experiments to search and screen for other sequences encoding ilvBNC or ilvD, the specification does not describe and define any structural features and amino acid sequences commonly possessed by each genus. Thus, one skilled in the art cannot visualize or recognize the identity of the members of each genus for use in the claimed method.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definitions, such as the structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v, Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), quoting *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe the genus of genetic materials, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g. structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. Therefore, the instant claims are not adequately described.

In view of the above considerations, one of skill in the art would not recognize that applicants were in possession of a genus of ilvD genes, a genus of ilvBN genes, a genus of ilvC genes, genus of panB genes, a genus of panC genes, a genus of pane genes, and a genus of panD genes

In regard to regulatory elements, such as promoters and repressor binding regions, and untranslated regions as encompassed by the term "gene", the examiner maintains that there is no correlation between these gene elements and the actual coding region of the gene. These elements are empirically determined. The specification does not provide a written description for these gene elements for each of the encompassed genus of ilvD genes, genus of ilvBN genes, genus of ilvC genes, genus of panB genes, genus of panC genes, genus of pane genes, and genus of panD genes. Thus, one of skill in the art would not recognize that applicants were in possession of the gene elements of each respective genus.

4. Claims 14-18, 20-26, 30-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated microorganism transformed with a gene construct containing SEQ ID NO: 1 and SEQ ID NO:2, and a method for producing L-valine using said isolated microorganism; does not reasonably provide enablement for any other embodiment.

Applicants' arguments filed 03/25/2005 have been fully considered and are persuasive in part. The examiner agrees that codon usage can be optimized to overcome problems with expression in particular microorganism host cells; thus, this particular ground of rejection has been withdrawn. However, the examiner respectfully disagrees with applicants' arguments that the specification provides enablement for the invention in view of the specification's teaching of using functional complementation to search for the recited genes for reasons of record as supplemented below.

The nature and breadth of the claims encompass any microorganism transformed with any gene construct containing any ilvD and/or ilvBNC gene of any nucleotide sequence from any biological source not limited to *Corynebacterium*, have any nucleotide sequence and structure, and include all variants and mutants thereof. The claims also encompass any method for making L-valine using a microorganism with any mutation of the endogenous gene encoding ilvD.

While the specification discloses a dihydroxy acid dehydratase of SEQ ID NO: 2 encoded by SEQ ID NO: 1, ketopantoate hydroxymethyl transferase of SEQ ID NO: 4 encoded by SEQ ID NO: 3, and pantothenate ligase of SEQ ID NO: 5 encoded by SEQ ID NO: 3 from *Corynebacterium glutamicum;* screening and searching for the recited genes from additional biological sources with differing nucleotide sequence and structures using functional

complementation is not guidance for making the claimed invention. Such procedure is a trial and error type of experimentation which is outside the realm of routine experimentation. Furthermore, searching and screening for any mutation to any endogenous gene encoding ilvD gene that will result in increased activity of ilvD is a trial and error type of experimentation which is outside the realm of routine experimentation.

The Examiner finds that one skilled in the art would require additional guidance, such as information regarding the specific nucleotide sequence of and biological source of the ilvD or ilvBNC gene. Without such guidance, the experimentation left to those skilled in the art is undue.

Conclusion

5. No claims are allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

7. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF

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